PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
C07D 215/14, A61K 31/33, 31/19, A61P 43/00, C07D 401/12, 401/14, 215/18, 405/12, 263/32, 213/30, 241/42, 277/24, 261/08, 271/06, 277/64

A1

(11) International Publication Number: **WO 00/64876**

(43) International Publication Date: 2 November 2000 (02.11.00)

(21) International Application Number: PCT/US00/11490

(22) International Filing Date: 28 April 2000 (28.04.00)

(30) Priority Data:
60/131,454 28 April 1999 (28.04.99) US

(71) Applicant *(for all designated States except US)*: AVENTIS PHARMACEUTICALS PRODUCTS INC. [US/US]; 500 Arcola Road, Collegeville, PA 19426 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: JAYYOSI, Zaid [FR/US]; 108 Cherrywood Court, Collegeville, PA 19426 (US). MCGEEHAN, Gerard, M. [US/US]; 1711 Spring House Road, Chester Springs, PA 19425 (US). KELLEY, Michael, F. [US/US]; 1086 Heartsease Drive, West Chester, PA 19382 (US). LABAUDINIERE, Richard, F. [FR/US]; 220 Richard Way, Collegeville, PA 19426 (US). ZHANG, Litao [US/US]; 456 Shakespere Drive, Collegeville, PA 19426 (US). CAULFIELD, Thomas, J. [US/US]; 362 Vista Drive, Phoenixville, PA 19460 (US). MINNICH, Anne [US/US]; 2107 Goodwin Lane, Montgomeryville, PA 19454 (US). BOBKO, Mark [US/US]; 526 Summercroft Drive, Exton, PA 19341 (US). MORRIS, Robert [US/US]; 125 Conestoga Road, Wayne, PA 19087 (US). GRONEBERG, Robert, D. [US/US]; 4173 Ironbridge Drive, Collegeville, PA 19426 (US). MCGARRY, Daniel, G. [GB/US]; Apt. 1148, 3000 Valley Forge Circle, King of Prussia, PA 19406 (US).

(74) Agents: OEHLER, Ross, J. et al.; Aventis Pharmaceuticals Products Inc., 500 Arcola Road, Collegeville, PA 19426 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: TRI-ARYL ACID DERIVATIVES AS PPAR RECEPTOR LIGANDS

(57) Abstract

This invention is directed to triaryl acid derivatives of formula (I) and their pharmaceutical compositions as PPAR ligand receptor binders. The PPAR ligand receptor binders of this invention are useful as agonists or antagonists of the PPAR receptor. In formula (I), (a), (b), and (c) are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkemyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl; A is –O–, –S–, –SO–, $-SO_2-$, $-NR_{13}-$, –C(O)–, $-N(R_{14})C(O)-$, $-C(O)N(R_{15})-$, $-N(R_{14})C(O)N(R_{15})-$, $-C(R_{14})=N-$, (d), (e), (f) a chemical bond, (g) or (h); B is –O–, –S–, –SO–, $-SO_2-$, $-NR_{17}-$, a chemical bond, ethynylene, –C(O)–, $-N(R_{18})C(O)-$, or $-C(O)NR_{18}-$; D is –O–, –S–, $-NR_{19}-$, a chemical bond, ethynylene, –C(O)–, $-N(R_{20})C(O)-$, or $-C(O)N(R_{20})-$; E is a chemical bond or an ethylene group; Z is $R_{21}O_2C-$, $R_{21}OC-$, cyclo-imide, –CN, $R_{21}O_2SHNCO-$, $R_{21}O_2SHN-$, $(R_{21})_2NCO-$, $R_{21}O$–2,4–thiazolidinedionyl, or tetrazolyl.